

**Rationale for the Development of
Ontario Air Standards
For
Acetonitrile**

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**Standards Development Branch
Ontario Ministry of the Environment**

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Executive Summary

The Ontario Ministry of the Environment (MOE) has identified the need to develop and/or update air quality standards for priority contaminants. The Ministry's Standards Plan, which was released in October, 1996 and revised in October, 1999, identified candidate substances for which current air quality standards will be reviewed over the next several years. Acetonitrile was identified as a priority compound for review due to the lack of an existing standard and its use in a variety of industrial processes. A review of scientific and technical information relevant to setting an air quality standard for acetonitrile has previously been provided to stakeholders for their comments. This Rationale document provides the rationale for recommending an Ambient Air Quality Criterion (AAQC) and Point of Impingement (POI) standard for acetonitrile.

Acetonitrile, CAS # 75-05-8, is a volatile, colourless, highly polar liquid. Due to its polarity, acetonitrile is used as a solvent to extract fatty acids and animal and vegetable oils. The petrochemical industry uses acetonitrile for extractive distillation due to its selective miscibility with organic compounds. Acetonitrile is also used as a solvent for polymer spinning and casting. Another common use of acetonitrile is as a starting material or catalyst for the syntheses of various chemicals. Manufacturers of pesticides, pharmaceuticals, perfumes, and nitrile rubber also use acetonitrile as an intermediate ingredient.

Acetonitrile may be released into the environment as a result of industrial uses. Data from the 2001 National Pollutant Release Inventory (NPRI) of Environment Canada indicated that all acetonitrile emissions were to air. The NPRI report indicates that emissions of acetonitrile have been declining since 1995. Total emissions in Canada for the years of 1995, 1996, 1997, 1998, 1999, 2000 and 2001 were 79.04, 23.7, 11.18, 8.17, 8.3, 6.39 and 6.14 tonnes, respectively. In 2001, sources in Ontario contributed more than 99% of the national atmospheric releases of acetonitrile. Neither Environment Canada nor the MOE monitors ambient air routinely for acetonitrile.

The exposure and absorption of acetonitrile occurs primarily through inhalation and secondarily through ingestion or dermal contact. The mechanism of acetonitrile toxicity has not been fully determined. Acetonitrile is metabolized to inorganic cyanide which can then be further oxidized to produce thiocyanate, a less toxic metabolite that can interfere with thyroid function. Acetonitrile is eliminated by exhalation of the unchanged compound and urinary excretion of free and bound hydrogen cyanide or acetonitrile. Thiocyanates are also eliminated by urinary excretion. Symptoms of acute exposure to acetonitrile include nausea, irregular respiration, and impaired motor activity. Human data regarding the chronic toxicity of acetonitrile are limited. Humans who are

chronically exposed to acetonitrile may suffer from headaches, anorexia, dizziness, weakness, nausea, flushing face and dermatitis.

The US EPA, in its carcinogen classification scheme, has listed acetonitrile as a Group D compound, which means there is insufficient data to draw any conclusion regarding its carcinogenicity to humans. The American National Toxicology Program recently examined the carcinogenicity of acetonitrile in rats and mice, based on 13-week and 2-year exposures, and concluded that the causal relationship between acetonitrile exposure and liver neoplasia is uncertain.

Ontario does not currently have ambient air quality standards for acetonitrile. In developing air quality standards for acetonitrile the Ministry of the Environment is considering risk assessments and standards and guidelines developed by: the United States Federal Government; the States of California, New York, New Jersey, Michigan and the Commonwealth of Massachusetts; the World Health Organization; the Netherlands; the Swedish Institute of Environmental Medicine and the Canadian Federal Government.

Only four of the agencies reviewed have ambient air quality criteria for acetonitrile. The United States Environmental Protection Agency (US EPA) has established a reference concentration (RfC) of $60 \mu\text{g}/\text{m}^3$ (micrograms per cubic metre), based on studies in mice. Michigan has adopted the inhalation RfC of the US EPA, as an Initial Threshold Screening Level, averaged over 24 hours. New York State's current Annual Guideline Concentration of $60 \mu\text{g}/\text{m}^3$ is also derived from the US EPA RfC. New Jersey adopted the US EPA's RfC of $60 \mu\text{g}/\text{m}^3$ as their reference concentration for inhalation. After reviewing additional toxicological information, the Ministry has chosen to derive Ontario's Air Quality Standards based on the LOAEL identified in the study by Pozzani *et al.*, (1959). Adverse effects on the respiratory system were identified in this study. The Ministry further considers that the subchronic mouse study, which forms the basis of the US EPA's RfC, provides further support to the resulting standard.

Based on an evaluation of the scientific rationale of air guidelines from leading agencies and an examination of current toxicological research, the Ministry is proposing the following air quality standards for acetonitrile (75-05-8):

- A 24-hour average AAQC of $70 \mu\text{g}/\text{m}^3$ (micrograms per cubic metre of air) based on the adverse respiratory effects of this compound; and
- A half-hour Point of Impingement standard of $210 \mu\text{g}/\text{m}^3$ (microgram per cubic metre of air) based on the adverse respiratory effects of this compound.

After consultation on these proposed standards, the Ministry's intent is to arrive at a decision regarding the effects-based AAQCs and the corresponding effects-

based POI standards. The standards (as opposed to guidelines) will then be incorporated into Regulation 346.

Meeting this proposed standard immediately may not be possible due to implementation issues related to economic/technical feasibility and the required timeframe to establish appropriate emission control technology. These implementation issues will be dealt with under the proposed Risk Management Framework for Air (under development) that is intended to address issues such as time, technology and economic considerations. The framework will provide a balance between effective, equitable and timely implementation of new or revised air quality standards while providing a mechanism to address implementation issues.

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1.0 Introduction

Ontario regulates air emissions in order to achieve and maintain air quality which is protective of human health and the environment. The *Environmental Protection Act* (Section 9) requires that all stationary sources that emit, or have the potential to emit, a contaminant obtain a Certificate of Approval which outlines the conditions under which the facility can operate.

The Ministry of the Environment uses a combination of regulated point of impingement (POI) standards and point of impingement guidelines, each of which is derived by mathematical scaling from an ambient air quality criterion (AAQC) (MOE, 2001) in reviewing Certificates of Approval. Ambient Air Quality Criteria represent human health or environmental effects-based values, and are normally set at a level not expected to cause adverse effects based on continuous exposure. As such, socio-economic factors, such as technical feasibility and costs, are not explicitly considered when establishing AAQCs.

Point of impingement standards are scheduled in Regulation 346 and can be used directly as compliance and enforcement tools. The regulation (Section 5(3)) specifies that a source cannot, "cause or permit the concentration of a contaminant at a point of impingement to exceed the standard prescribed in Schedule 1". All sources are required to comply with the standards in Regulation 346 unless there is a more recent or site specific legal instrument that provides other direction to a facility. Dispersion modelling (Section 5(2) and the referenced Appendix in Regulation 346), which incorporates detailed engineering calculations, is used to relate emission rates from a source to resulting ambient concentrations of a particular contaminant at the maximum POI. Since POI standards specified under Regulation 346 apply to all stationary sources, implementation issues need to be considered to ensure that the standards are technically feasible, and that there is a balance between the risks and the costs of improved ambient air quality. Implementation issues will be considered by the proposed Risk Management Framework for Air (under development).

In addition to POI standards established under Regulation 346, the Ministry also has a large number of POI guidelines. These are used by the Ministry to assess general air quality, and the *potential* for causing adverse effect (MOE, 2001). Like the POI standards specified in Regulation 346, POI guidelines are used in reviewing applications for Certificates of Approval, to approve new and modified emission sources. Once incorporated into a legal instrument such as a Certificate of Approval, POI guidelines are legally binding. However, unlike POI standards in Regulation 346, guidelines are subject to appeal.

The Ontario Ministry of the Environment has identified the need to develop and/or update air guidelines/standards for priority toxic contaminants. The Ministry's Standards Plan, which was released in October 1996 and revised in October 1999 (MOEE, 1996 & MOE, 1999), identified candidate substances for which current air standards will be reviewed, over the next several years. In March 1998, following the 1996 initiative, the Ministry proposed a multi-step process for developing air quality standards (MOE, 1998). As an initial step, risk assessment information relevant to establishing a standard for a particular compound was documented and made available for stakeholder review. This provided stakeholders with the opportunity to critically review the information and provide any additional information they felt should be considered by the Ministry in setting an air quality standard for a particular compound.

Acetonitrile was identified as a priority due to the lack of an existing standard and its use in a wide variety of industrial processes. A review of scientific and technical information relevant to setting an ambient air quality standard for acetonitrile has been provided in a previous document, and was distributed to stakeholders for their comments. This Rationale document therefore provides the rationale for recommending an AAQC and a POI standard for acetonitrile.

2.0 General Information

2.1 Physical and Chemical Properties

Acetonitrile is a volatile, colourless, highly polar liquid with a sweet, ether-like odour. It is extremely soluble in water and miscible with ethanol, ether, acetone, chloroform, carbon tetrachloride, and ethylene chloride (WHO, 1993). The Canadian Centre for Occupational Health and Safety (CCOHS, 1996) classifies acetonitrile as a flammable and combustible material.

A wide range of odour thresholds have been identified in the literature which span several orders of magnitude. These values range from 330 (Vershueren, 1983) to 285,000 $\mu\text{g}/\text{m}^3$ (Aamore and Hautala, 1983, US EPA, 1995). Due to the range of study quality, design, and reporting, the American Industrial Hygiene Association (AIHA) conducted a review of existing compilations of odour criteria and developed a number of conditions for acceptance of an odour impact study (AIHA, 1989). The AIHA recommends that the odour threshold be established at the geometric mean of the range of values from studies meeting the conditions of acceptability. In the case of acetonitrile, the AIHA indicated that only one study demonstrated acceptable testing conditions (Dravnieks, 1974). Dravnieks (1974) determined an odour threshold of 1950 $\mu\text{g}/\text{m}^3$ for acetonitrile. The following list

provides some specific information on acetonitrile and its properties (CCOHS, 1996; Hartung, 1994; WHO, 1993):

CAS #	75-05-8
RTECS #	AL7700000
UN #	1648
Conversion Factors:	1 ppm = 1.68 mg/m ³ 1 mg/m ³ = 0.595 ppm @ 25 °C and 103 kPa
Melting Point	-43 +/- 2 °C
Boiling Point	81.6 °C
Flash Point	12.8 °C - closed cup, 6 °C -open cup
Henry's Law Constant	2.93 x 10 ⁻⁵ atm-m ³ /mole
Log K _{ow}	-0.34
Water Solubility	Infinitely soluble in water; (readily miscible with alcohol, ether, acetone, chloroform)
Formula	CH ₃ CN
Molecular weight	41.05
Vapour density (air=1)	1.42
Vapour pressure	74 mm Hg at 20 °C
Common synonyms	Cyanomethane, ethyl nitrile, methyl cyanide

2.2 Uses

Acetonitrile, a highly polar solvent, is used to extract fatty acids as well as animal and vegetable oils. The petrochemical industry uses acetonitrile for extractive distillation due to its selective miscibility with organic compounds. Acetonitrile is also used as a solvent for polymer spinning and casting. The syntheses of many chemicals such as acetophenone, alpha-naphthalenacetic acid, thiamine, and acetamidine use acetonitrile as a starting material or catalyst. Manufacturers of pesticides, pharmaceuticals, perfumes, and nitrile rubber also use acetonitrile as an intermediate ingredient.

2.3 Sources and Levels

Primarily anthropogenic in nature, acetonitrile is a by-product from the manufacture of acrylonitrile (US EPA, 1994) and coal tar production. Acetonitrile is also formed during combustion of wood, straw, and other vegetation. Automobile exhaust (US EPA, 1983) and tobacco smoke also contain acetonitrile.

Although acetonitrile has a variety of industrial uses as a solvent or starting material, it is generally released into the environment by direct discharges to air or by leaching into underground sites. It may be released from the thermal combustion of polyurethane foams or from municipal waste treatment plant discharges or spills. As acetonitrile is a component of tobacco smoke, human exposure often results from indoor levels rather than outdoor levels. Data from the 2001 National Pollutant Release Inventory (NPRI) of Environment Canada indicated that all acetonitrile emissions were to air. NPRI data show that acetonitrile emissions have been declining since 1995. On-site releases for 1995, 1996, 1997, 1998, 1999, 2000 and 2001 were 79.04, 23.70, 11.18, 8.17, 8.30, 6.39 and 6.14 tonnes, respectively (NPRI 1995; 1996; 1997; 1998; 1999; 2000; 2001). In 2001, sources in Ontario contributed more than 99% of the national atmospheric releases of acetonitrile. The majority of emissions were from the chemical and chemical products industry.

Neither Environment Canada nor MOE routinely monitor ambient air for acetonitrile therefore, the average ambient levels of acetonitrile in Ontario are unknown. Canadian facilities do not measure acetonitrile routinely or during special trace gas studies (Dann, 1997). In a rural area of the United States, air sampling of acetonitrile over a 24-hour period showed daily means of $0.08 \mu\text{g}/\text{m}^3$ (US EPA, 1987). A single sampling done in an urban area of the United States reported acetonitrile concentrations below the detection limit; however, the World Health Organization (WHO) reported air concentrations in both urban and rural areas range from 3.36 to $11.96 \mu\text{g}/\text{m}^3$ (WHO, 1993). Acetonitrile levels sampled in air at a rural site before and after burning of brush and grass increased from 6.7 to $58.7 \mu\text{g}/\text{m}^3$. Becker *et al.* (1982) reported concentrations of up to $12.4 (\pm 4.0) \mu\text{g}/\text{m}^3$ at a city centre in Germany.

A sample of eight facilities emitting acetonitrile was identified from an analysis of recent applications for Certificates of Approval (C of A) in Ontario. These approvals were for emissions from a variety of industries involved with coating and bonding agents and the pharmaceutical industry. The median Ground Level Concentration (GLC) estimated by Regulation 346 dispersion modelling for the eight sources was approximately $73 \mu\text{g}/\text{m}^3$ averaged over a half-hour. The minimum and maximum GLCs were 1.58 and $214 \mu\text{g}/\text{m}^3$, respectively.

2.4 Environmental Fate

The primary atmospheric removal processes of acetonitrile include reactions with hydroxyl, or other free radicals, and with ozone (US EPA, 1985). Acetonitrile persists in air with an estimated half-life ranging from approximately 20 to 54 days. Reaction with hydroxyl radicals is the major mechanism for the removal of acetonitrile from the atmosphere with an estimated half-life of up to 20 days. Reaction with ozone is slower with an estimated half-life of up to 54 days. Reactions between chlorine radicals and acetonitrile are not believed to be significant compared with hydroxyl radical reactions (Arjis *et al.*, 1983). Direct photolysis in the ambient atmosphere is not a likely removal process as acetonitrile does not absorb light at wavelengths greater than 160 nm.

Wet deposition is the most significant physical atmospheric removal process because acetonitrile is very soluble in water, resulting in dissolution into clouds and raindrops and subsequent removal by rainfall. Dry deposition and adsorption on aerosol particles are not expected to be significant removal mechanisms (US EPA, 1985). Acetonitrile is predicted to have low soil sorption and is removed from soils by microbial degradation or evaporation (US EPA, 1987).

At 20-25 °C, the half-life of acetonitrile in natural waters is estimated to be 1 to 2 weeks, based on biodegradation data for river water and volatility estimates (US EPA, 1987). Volatilization is anticipated to be significant for most water bodies, but may not be rapid due to the high water solubility and moderate vapour pressure and low Henry's Law constant. Experimental data pertaining to the adsorption of acetonitrile to particulate organic matter and suspended sediment in water are limited, but the high water solubility of acetonitrile suggests that partitioning from the water column to sediments will be insignificant.

3.0 Toxicology of Acetonitrile

The following toxicological review of acetonitrile is primarily focussed on the inhalation route of exposure. Inhalation is the predominant pathway of human exposure due to the relatively volatile nature of acetonitrile and the fact that most releases of the chemical are to air. Data on other exposure media are included where relevant, or where inhalation data are lacking.

Acetonitrile is metabolized to inorganic cyanide, this reaction however occurs at a much slower rate compared with other nitriles. The mechanism of acetonitrile toxicity has not been fully elucidated, but it is believed to be similar to the reaction of inorganic cyanide with cytochrome oxidase in the mitochondria which leads to cellular anoxia.

Although data are limited, acetonitrile appears to be well absorbed following inhalation. A study of cigarette smokers who inhaled cigarette smoke indicated that 91% of the inhaled acetonitrile was retained by the body (Dalhamn *et al.*, 1968a). The retention rate decreased to 74% when the smoke was not inhaled but held in the mouth for 2 seconds prior to exhaling (Dalhamn *et al.*, 1968b). A study utilizing three beagle dogs as test subjects found that acetonitrile is absorbed rapidly upon inhalation and that steady-state blood concentrations were reached 3 to 4 hours after exposure (Pozzani *et al.*, 1959). Dequidt *et al.* (1974) conducted an examination of a human subject subsequent to the inhalation of a fatal dose of acetonitrile and found that acetonitrile was uniformly distributed within the internal organs and that cyanide metabolites were found in the spleen, stomach, and skin. Lower levels of metabolites were found in the liver, lungs, kidneys, heart, brain, muscle, intestines, and testes. An earlier study of a subject, also exposed to a fatal dose of acetonitrile by inhalation, found high levels of cyanide ion in the blood, urine, kidney, spleen and lungs, but not in the liver (Grabois, 1955). In mice dosed with radiolabelled acetonitrile the highest levels of radioactivity were found in the liver and kidney 5 minutes after dosing. The levels in those organs then declined with time. Twenty-four and 48 hours later radioactivity was highest in the gastrointestinal tract, thymus, liver and testes. In the liver 50% of the radioactivity was bound to macromolecular fractions while in other organs it was found primarily in the lipid fractions. (Ahmed *et al.*, 1992).

There are no specific studies describing acetonitrile biotransformation and elimination in humans, however, accidental poisoning cases indicate that acetonitrile is transformed into cyanide and then thiocyanate. Acetonitrile is eliminated by exhalation of the unchanged compound and urinary excretion of free and bound hydrogen cyanide or acetonitrile (US EPA, 1985). Thiocyanates, oxidation products of cyanide, are also eliminated through urinary excretion. Acetonitrile (22 to 200 µg/L) was also found in the morning urine of heavy cigarette smokers (McKee *et al.*, 1962). Acetonitrile was shown to be converted to cyanide by rat nasal and liver tissues with the maximum rate being ten times higher per gram of protein in the nasal tissue than in any other tissue monitored (ACGIH, 2002).

3.1 Acute Toxicity

Symptoms of acute exposure to acetonitrile in occupational settings include nausea, irregular respiration, and impaired motor activity. Respiratory irritation has been reported at 840,000 µg/m³ (CCOHS, 1996), and bronchial constriction and tightness in the chest occurs at 268,000 µg/m³ (NIOSH, 1989). At high doses, it can produce acute health effects such as nose and throat irritation (CCOHS, 2000) and in extreme cases of exposure, death can occur quickly from respiratory failure. A worker who died shortly after an acute exposure of an unknown concentration of acetonitrile demonstrated cerebral, thyroid, liver, splenic, and renal congestion (WHO, 1993).

A human inhalation exposure study was conducted in a clinical setting by Pozzani *et al.* (1959), with three male volunteers. Four hour exposures to 40, 80 and 160 ppm (67,000, 134,000 and 268,000 $\mu\text{g}/\text{m}^3$) acetonitrile were conducted with increasing recovery time allowed between exposures as the concentration increased. Two of the men exposed to 40 ppm (67,000 $\mu\text{g}/\text{m}^3$) showed no apparent adverse effects and levels of blood cyanide and urinary thiocyanate did not increase significantly. The third participant in the trial who was exposed to the same conditions demonstrated chest tightness and a cooling sensation in the lungs in the evening following exposure, while the cooling sensation was also experienced the following morning and persisted for approximately 24 hours. This participant also demonstrated an increase in urinary thiocyanate concentration but not in blood cyanide levels. All three participants experienced olfactory fatigue after two to three hours of exposure. One week later the two men who did not experience any adverse effects, during the first exposure, were exposed to 80 ppm (134,000 $\mu\text{g}/\text{m}^3$). Again, these men did not report any adverse subjective responses. Nine days later, these two men were again exposed to 160 ppm (269,000 $\mu\text{g}/\text{m}^3$). This time one of the men experienced a slight flushing of the face two hours after inhalation and chest tightness five hours later. Blood cyanide and urinary thiocyanate levels did not change significantly for either subject.

LC₅₀'s (concentration lethal to half of the test animals) of 4.8 to 9.5 mg/m^3 have been reported in some animal species (mice, guinea pigs, rabbits) following 4 to 14-hours of exposure (US EPA, 1985).

3.2 Subchronic/Chronic Toxicity

Human data regarding the chronic toxicity of acetonitrile are limited. Humans who are chronically exposed to acetonitrile may suffer from headaches, anorexia, dizziness, weakness, nausea, flushing of the face and dermatitis (Hazardous Substances Database, 1994).

The most relevant studies regarding long term exposure through inhalation are those conducted under the American National Toxicology Program (NTP, 1996). Six groups of mice were exposed to acetonitrile by inhalation at concentrations of 0, 100, 200, 400, 800 or 1,600 ppm (approximately: 0, 170, 340, 670, 1,340, or 2,690 mg/m^3) for 6 hours a day, 5 days a week for 13 weeks. Mortality was observed at concentrations of 670 mg/m^3 or higher. All of the mice in the group exposed to 2,690 mg/m^3 , died by the fourth week of the study. Effects from chronic exposure included increased liver weight and increased incidences of forestomach hyperplasia. Hepatocellular vacuolization was observed in all groups except the mice in the highest concentration group that died, the investigators concluded that vacuolization represented the storage of glycogen and was not considered to be an adverse effect. Forestomach hyperplasia is considered to be an adverse effect as it is associated with an increase of

inflammatory cells and focal ulcers (at the highest concentrations in female mice). However, the role of inhalation on the development of forestomach hyperplasia is not clear as these types of lesions were observed in other NTP inhalation studies, suggesting that the effect may not be directly related to acetonitrile exposure but rather the conditions of exposure routes such as grooming of contaminated fur or mucociliary clearance followed by ingestion (NTP, 1996). Based on this study with mortality as an endpoint, the no-observed-adverse-effect-level (NOAEL) was found to be 340 mg/m³ (NOAEL adjusted for continuous exposure duration = 60 mg/m³). A similar 13-week study was conducted on rats, but due to limited histopathological observations in the lower concentration groups, the results were insufficient to identify a NOAEL (NTP, 1996).

The American National Toxicology Program also conducted an 111-week study on four groups of mice exposed to acetonitrile by inhalation at concentrations of 0, 50, 100, and 200 ppm (approximately 0, 85, 170, or 340 mg/m³) for 6 hours a day, 5 days a week. Clinical signs and body weight were monitored throughout the study, but hematological parameters were not studied. No differences in survival, body weight, or liver weight were observed between the treated mice and the control groups. Forestomach hyperplasia was observed to increase significantly at the 340 mg/m³ concentration in male mice; and, at both 170 and 340 mg/m³ concentrations in female mice. However, neither a NOAEL nor a lowest-observed-adverse-effects-level (LOAEL) was determined from this study, due to the uncertainty of the cause of the forestomach lesions. In a similar two-year study on groups of rats exposed to 0, 100, 200, and 400 ppm (approximately 0, 170, 340, and 680 mg/m³), no adverse effects were found. Therefore, a NOAEL of 400 ppm or 680 mg/m³ (NOAEL adjusted for continuous exposure duration = 120 mg/m³) was identified for the rat (NTP, 1996).

3.3 Developmental / Reproductive Toxicity

There are no data reported in the literature regarding the developmental / reproductive effects of acetonitrile in humans.

Willhite (1983) suggested that acetonitrile is fetotoxic in rats and teratogenic in Syrian Golden hamsters. Pregnant hamsters were given a single oral dose of acetonitrile on the eighth day of gestation. At 200,000 µg/kg, acetonitrile caused a dose-related increase in early resorption and fetal death in hamsters, rats, and rabbits. The gavage of hamsters at higher doses caused an increase in the incidence of malformed offspring.

In a study conducted by Argus Research Laboratories (1984), pregnant rabbits given oral doses of acetonitrile on gestation days 6 through 18 at levels of 0, 2, 15, and 30 mg/kg/day, showed anorexia and decreased body weight gain; and death occurred in 5 out of 25 rabbits at the highest dose. Fetal toxicity was

observed at the highest dose level; therefore, the World Health Organization does not consider acetonitrile to be toxic to fetuses at doses below those causing maternal toxicity based on this study (WHO, 1993). This conclusion has also been supported by an inhalation study of pregnant rats exposed to 100, 400, or 1200 ppm (168,000, 672,000 or 201,600 $\mu\text{g}/\text{m}^3$) of acetonitrile for six hours per day on gestation days 6 through 19 (NTP, 1994). In this latter study, several rats died at the higher concentrations, despite the absence of significant effects on maternal body weight or incidence of fetal malformations. Significant acetonitrile concentrations were detected in maternal blood and cyanide was also found to be present in the blood of the 1200 ppm group. A NOAEL of 168,000 $\mu\text{g}/\text{m}^3$ for maternal toxicity was determined for Sprague-Dawley rats.

3.4 Genotoxicity

Acetonitrile did not cause gene mutations in the Ames assay (*Salmonella typhimurium*) with or without S9 metabolic activation enzymes (HSDB, 1994; NTP, 1996). Hydrogen cyanide, a metabolite of acetonitrile, has been found to be a direct-acting mutagen in a *Salmonella typhimurium* assay. However, in Chinese hamster ovary cells, acetonitrile produced a weakly positive response in the sister chromatid exchange assay without S9 metabolic enzymes and caused chromosomal aberrations in the assay with the S9 metabolic enzymes (NTP, 1996). Acetonitrile has not been shown to cause gene mutations in either bacteria or cultured mammalian cells, but does cause chromosomal aberrations. Acetonitrile was found to be a highly effective aneuploidogen, causing both chromosome gain and loss, following a short exposure of fruit flies (*Drosophila melanogaster*) to 131 ppm (220 mg/kg) acetonitrile (Osgoode *et al.*, 1991).

3.5 Carcinogenicity

The US EPA, in its carcinogen classification scheme, has listed acetonitrile as having insufficient information to classify (Group D). In other words, there is insufficient data to draw any conclusion regarding its carcinogenicity to humans. A recent study examined the carcinogenicity of acetonitrile to rats and mice exposed for durations of 13-weeks or 2-years (NTP, 1996). The 2-year inhalation study showed some evidence of carcinogenic activity of acetonitrile in male rats, but no such evidence for mice or female rats were found. Although a significant trend of increased incidence of hepatocellular adenomas was observed, the incidences were not considered to be statistically significant by pairwise comparison. The study suggested that the causal relationship between acetonitrile exposure and liver neoplasia in male rats is uncertain.

3.6 Environmental Effects

Acetonitrile released to surface water will volatilize. Due to high water solubility and a low octanol-water partitioning coefficient, acetonitrile is not expected to bioaccumulate in aquatic organisms. A bioconcentration factor of 0.3 has been estimated for acetonitrile (US EPA, 1985). Acetonitrile is not highly toxic to *Daphnia magna* (48-hour LC_{50} = 3,600,000 $\mu\text{g/L}$) (Tong *et al.*, 1996). The 96-hour LC_{50} values for several fish species range from 1,650,000 $\mu\text{g/L}$ to 1,850,000 $\mu\text{g/L}$ (Henderson *et al.*, 1961; Brooke *et al.*, 1984). Acetonitrile is expected to biodegrade in soil in experiments using the microorganism, *Nocardia rhodochrus*. Results showed acetonitrile concentrations in the test medium were decreased by 52% in eight hours (DiGeronimo *et al.*, 1976).

4.0 Review of Existing Air Quality Criteria

4.1 Overview

Currently Ontario does not have ambient air quality criteria for acetonitrile. Documentation outlining the basis of air quality criteria for acetonitrile from the following ten agencies was reviewed: the United States Federal Government; the States of California, New York, New Jersey, Michigan and the Commonwealth of Massachusetts; the World Health Organization, the Netherlands, the Swedish Institute of Environmental Medicine and the Canadian Federal Government in developing an air standard for Ontario. A brief summary of available criteria is presented in Table 1. Agency specific summaries of air quality guidelines are presented in Section 11.

In reviewing the air quality guidelines and exposure limits presented in Table 1, it should be noted that the Ministry of the Environment typically uses a factor of **15** to convert from guidelines based on annual average concentrations to half-hour point-of-impingement limits and a factor of **3** to convert from guidelines based on 24-hour average concentrations. These factors are derived from empirical measurements and are selected to ensure that if the short-term limit is met, air quality guidelines based on longer-term exposures will not be exceeded (MOE, 1994; MOE, 1987).

Table 1: Summary of Existing Air Quality Guidelines for Acetonitrile

Agency	Guideline Value	Basis of Guideline	Date ¹	Comments
Canada (CEPA)	No guideline listed.		1993	Not on PSL-1 or PSL-2
Ontario (MOE)	No guideline listed.			
US EPA (IRIS)	60 µg/m ³ (Chronic RfC)	13-week mouse inhalation study, mortality endpoint	1999	Inhalation reference concentration (RfC)
California (OEHHA)	No guideline listed.			
Florida (DEP)	No guideline listed.			
Massachusetts (DEP)	No guideline listed.			
Michigan (DEQ)	60 µg/m ³ (24-hour ITSL)	RfC from US EPA	2001	Permitting standard, i.e., the Predicted Ambient Impact of a toxic from any facility cannot exceed its screening level
New Jersey (DEP)	60 µg/m ³ (annual average)	13-week mouse mortality study	2003	US EPA RfC (1999)
New York (DEC)	60 µg/m ³ (annual AGC)	Based on the US EPA's RfC	2000	Annual Guideline Concentration

¹ Date here refers to when the health-based guideline background report or original legislative initiative was issued. The sources were the respective agency documents.

Agency	Guideline Value	Basis of Guideline	Date ¹	Comments
	10 000 µg/m ³ (1-hour acute SGC)	Based on the ACGIH-STEEL	2000	Short-term Guideline Concentration
North Carolina (DENR)	No guideline listed.			
Texas (NRCC)	No guideline listed.			
Netherlands	No guideline listed.			
Sweden	No guideline listed.			
WHO (Europe and PHE)	No guideline listed.			

¹ Guidelines in this table can refer to: guidelines, risk-specific concentrations based on cancer potencies, and non-cancer-based reference concentrations.

² Date here refers to when the health-based guideline background report or original legislative initiative was issued. The sources were the respective agency documents.

However, depending on the health endpoint being considered, other conversion factors may also be employed.

Of the agencies reviewed, the US EPA and the States of New York, New Jersey and Michigan have developed criteria or reference values for acetonitrile. The US EPA has developed an inhalation Reference Concentration (RfC) of $60 \mu\text{g}/\text{m}^3$ based on a chronic inhalation study of mice through the NTP (US EPA, 1999). New York and Michigan have 24-hour average limits of $60 \mu\text{g}/\text{m}^3$, based on the current US EPA (IRIS) RfC. The annual average for New Jersey is $60 \mu\text{g}/\text{m}^3$, based on the US EPA's RfC. California, Massachusetts, the Netherlands, the WHO, Sweden and the Canadian Federal Government have not established air quality guidelines for acetonitrile.

4.2 Evaluation of Existing Criteria

The current US EPA carcinogenic classification of acetonitrile is Group D (not classifiable), based on the weight-of-evidence judgement (US EPA, 1999). It is not classifiable due to the lack of human evidence and because the animal evidence is equivocal (i.e., composed of conflicting data). While the study done through the NTP showed evidence for carcinogenicity in male rats, no evidence was found in mice or female rats and although a significant trend of increased incidence of hepatocellular adenomas was observed, the incidences were not considered to be statistically significant by pairwise comparison. None of the agencies reviewed based their criteria on a carcinogenic endpoint.

Michigan has adopted the inhalation RfC ($60 \mu\text{g}/\text{m}^3$) for acetonitrile developed by the US EPA as an Initial Threshold Screening Level (ITSL), averaged over 24 hours (Searles, 1999). New York has also recently adopted the US EPA RfC in developing their Annual Guideline Concentration (AGC). The US EPA RfC of $60 \mu\text{g}/\text{m}^3$ is derived principally from a study conducted on mice under the National Toxicology Program (1996). A NOAEL of $340 \text{ mg}/\text{m}^3$ based on mortality was determined. Mortality was considered an appropriate endpoint as there were no observed nonneoplastic adverse effects clearly associated with inhalation exposure below those levels that resulted in mortality (400 ppm or $670 \text{ mg}/\text{m}^3$) (US EPA, 1999). The NOAEL was adjusted from the experimental exposure (6 hours for 5 days a week) to a continuous environmental exposure (24 hours for 7 days a week). Thus, a duration-adjusted concentration (ADJ) of the NOAEL ($\text{NOAEL}_{\text{ADJ}}$) of $60 \text{ mg}/\text{m}^3$ was obtained. Uncertainty factors applied to the $\text{NOAEL}_{\text{ADJ}}$ to obtain the RfC were $10^{1/2}$ to account for interspecies extrapolation, 10 for the protection of sensitive human subpopulations and $10^{1/2}$ for database deficiencies (lack of data on reproductive endpoints involving exposure of laboratory animals before and during mating through parturition and the absence of hematological measurements). Grooming of contaminated fur or mucociliary clearance with subsequent ingestion was likely a factor in the development of

forestomach lesions in the mice and so a modifying factor of 10 was applied to the $\text{NOAEL}_{\text{ADJ}}$ due to the uncertain role of inhalation exposure. Thus, an RfC of $60 \mu\text{g}/\text{m}^3$ was derived. Confidence in the principal study, the overall database of toxicological information and the inhalation RfC for acetonitrile is reported as medium by the US EPA. Although the NTP study (1996) utilized appropriate sample sizes, extensive histopathology and detailed data reporting format, haematological parameters were not measured in mice and only at the 15-month interim sacrifice in rats. The database was given a medium confidence rating because of the uncertain role of inhalation in the development of forestomach lesions in the mouse study, the lack of evaluation of possible effects of acetonitrile on heart rate, ventilatory parameters and blood pressure as well as the absence of two-generation studies. Since the confidence in both the principal study and the database are rated as medium, the confidence in the RfC is also considered medium.

New York State also has a Short-term Guideline Concentration (SGC) of $10,000 \mu\text{g}/\text{m}^3$ (1-hour acute value) derived from the American Conference of Governmental Industrial Hygienists Short-term Exposure Limit (ACGIH STEL, $100,000 \mu\text{g}/\text{m}^3$) divided by a factor of 10 to protect the general population which includes sensitive individuals, infants and the elderly. New York State is planning to move from the development of air quality guidelines to air quality regulations and plans to remove the Short-term Guideline concentration for acetonitrile in this process (Desantis, 1999).

New Jersey currently has an annual average of $60 \mu\text{g}/\text{m}^3$ which is derived from the US EPA RfC (New Jersey Department of Environmental Protection, 2003). The RfC of $60 \mu\text{g}/\text{m}^3$ is based on a 13-week inhalation study of mice. The endpoint used to derive this value was death with the NOAEL being 200 ppm. A total uncertainty factor of 100 and a modifying factor of 10 were applied to the NOAEL.

In 2001 the ACGIH placed acetonitrile on the Notice of Intended Changes list. In 2002 a TLV-TWA value of 20 ppm was adopted based on its effects in the lungs. The value was based on human data in which two of three volunteers showed no effects from exposure to 40 ppm. The third volunteer, however, experienced slight tightness in the chest and a sensation of cooling in the lungs.

5.0 Responses of Stakeholders to the Information Draft

In December 2002, the Ministry posted Information Draft documents for fifteen chemicals, including acetonitrile, for air standards development under the Standards Plan (MOEE, 1996; MOE, 1999) to the Environmental Registry. The Ministry requested input regarding: the completeness of relevant inhalation toxicological information examined by the Ministry; the rationales of the agencies that the Ministry has considered appropriate for the development of air quality standards; if the scientific rationale supporting the RfC developed by the US EPA provides the most appropriate basis on which to set an air quality standard or is an occupational exposure limit a more appropriate basis; and finally, does the range of effects noted from exposure warrant the uncertainty factors applied by the US EPA in deriving their RfC.

During the consultation period the Ministry did not receive any comments from stakeholders pertaining to acetonitrile specifically. However, several stakeholders indicated that they had general science and policy issue concerns for the overall air standards process. For more information on this, please refer to the "Other Relevant Information" section of the Environmental Registry Notice XA02E0007.

6.0 Overview of the Next Phase of the Ministry's Standards Setting Process

The first phase of the standards development process, the information draft, for acetonitrile is now complete. This phase provided stakeholders with an opportunity to comment on the toxicological and other scientific information used in the development of the air quality standard.

The Ministry is now soliciting comments from stakeholders regarding the proposed ambient air quality criteria and POI standard that are presented in Section 8.0 below. This is the next phase in the overall process of standards development. The goal of this phase is to arrive at a decision regarding the effects-based AAQCs and the corresponding effects-based POI standard for acetonitrile. If the proposed effects-based POI standard cannot be met immediately, this will be dealt with on a case-by-case basis under the proposed risk management framework for air (currently under development). In the meantime, the Ministry may propose an interim POI standard to ensure

continued environmental improvement while the risk management phase proceeds.

7.0 Considerations in the Development of an Ambient Air Quality Criterion for Acetonitrile

Acetonitrile is a volatile, colourless, highly polar liquid which is extremely soluble in water. The American Industrial Hygiene Association (AIHA) conducted an extensive review of odour thresholds reported in the literature. The odour threshold reported by Dravnieks, 1974 of $1950 \mu\text{g}/\text{m}^3$ was the only one which met their review criteria. Acetonitrile persists in the air with a half-life of 20 to 54 days. Currently there are no Ontario Ambient Air Quality Criteria for acetonitrile.

Acute inhalation exposure of acetonitrile may result in nausea, irregular respiration, and impaired motor activity. At high doses it can produce acute health effects such as nose and throat irritation. Respiratory irritation has been reported at $840\,000 \mu\text{g}/\text{m}^3$ and bronchial constriction and tightness in the chest occurs at $268\,000 \mu\text{g}/\text{m}^3$. Chronic exposure to acetonitrile may induce headaches, anorexia, dizziness, weakness, nausea, flushing of the face and dermatitis.

Of the agencies reviewed, the US EPA and the States of New York, New Jersey and Michigan have developed criteria or reference values for acetonitrile. The US EPA RfC is derived principally from a subchronic inhalation study on mice conducted through the NTP which defined a $\text{NOAEL}_{\text{ADJ}}$ of $60 \text{ mg}/\text{m}^3$. Mortality was chosen as the critical effect as adverse effects were not observed at exposure levels below those that resulted in death. The steep exposure-response relationship of acetonitrile is consistent with data for other cyanide-containing chemicals. The RfC incorporates adjustments for interspecies extrapolation, sensitive human subpopulations and database deficiencies for a combined uncertainty factor of 100. A modifying factor of 10 was also applied to account for the uncertain role that inhalation may play in causing forestomach lesions on the mice after exposure. New Jersey, New York and Michigan have adopted the RfC of $60 \mu\text{g}/\text{m}^3$ developed by the US EPA as an appropriate exposure limit for acetonitrile.

The toxicological review found many case reports for adverse effects in humans occurring following exposure to acetonitrile. The primary organ systems affected were respiratory, renal, hepatic, thyroid (gland) and central nervous system. There are also many reports of deaths as a result of occupational and accidental exposure. These observed effects in humans are consistent with those observed in experimental animals which also found the thyroid (gland), respiratory, hepatic and central nervous systems to be targets of toxicity. The Ministry considers that

the air quality standards established in this document will protect against those adverse effects. The AAQC is derived by applying the following uncertainty factors to the LOAEL of 67,000 $\mu\text{g}/\text{m}^3$ (40 ppm) observed in the human study by Pozzani *et al.*, 1959:

- I. 10 for intraspecies sensitivity;
- II. 10 for duration of study; acute versus chronic; and
- III. 10 for use of LOAEL instead of a NOAEL.

This results in a cumulative uncertainty factor of 1000. Converting to micrograms per cubic metre gives a value of 67 $\mu\text{g}/\text{m}^3$ which is then rounded to 70 $\mu\text{g}/\text{m}^3$ for the final 24-hour AAQC.

Further support for ambient air quality criterion at this level comes from the subchronic and chronic studies conducted in mice and rats by the NTP. Of these species it was determined that mice were most sensitive to the effects of acetonitrile. Because effects seen in the chronic study were ambiguous the subchronic study was used to derive reference exposure levels. In this 13-week study mortality was observed at exposures of 400 ppm and greater and so the NOAEL was determined to be 200 ppm.

To calculate a 24-hour AAQC using the NTP study the Ministry would apply the following uncertainty factors: 10 for each of intraspecies and interspecies differences, and 10 for database uncertainties. The uncertainty factor for database uncertainties accounts for issues such as: the relevance of forestomach hyperplasia to humans and the role of inhalation exposure in its etiology, all human data being from acute exposures and the lack of multi-generation reproductive studies. A total uncertainty factor of 1000 would be applied to a duration adjusted NOAEL of 36 ppm resulting in an AAQC of 60 $\mu\text{g}/\text{m}^3$.

Given that these two approaches produce AAQC's within such a close range the Ministry has chosen to apply greater weight to value derived from human data. It is also important to note that at this level odour is not expected to be a concern.

8.0 Recommendations

The Ministry of the Environment has reviewed and considered air quality guidelines and standards used by leading agencies world-wide and the science upon which these standards are based. Of the criteria reviewed the Ministry has chosen to base the standard on the LOAEL identified in the study by Pozzani *et al.*, (1959), with further support provided by the subchronic mouse study which

forms the basis of the US EPA's RfC. In the Pozzani *et al.*, (1959) study adverse effects on the respiratory system were experienced by human volunteers. Based on the information reviewed from leading agencies and the assessment of the available toxicological information, the Ministry is proposing the following:

- A 24-hour average AAQC of 70 µg/m³ (micrograms per cubic metre of air), based on the adverse respiratory effects of this compound, and;
- A half-hour Point of Impingement standard 210 µg/m³ (microgram per cubic metre of air) based on the adverse respiratory effects of this compound.

The Ministry of the Environment uses a factor of 3 to convert from criteria based on 24-hour average concentrations to half-hour POI standards. This factor is derived from empirical measurements and is selected to ensure that if the short-term limit is met, air quality standards based on longer-term exposures will not be exceeded (MOE, 1987; MOEE, 1994)

There may be incidences where meeting the proposed POI standard immediately may not be possible due to implementation issues related to economic/technical feasibility and the required timeframe to establish appropriate emission control technology. These implementation issues will be dealt with under the proposed Risk Management Framework for Air (currently under development) that is intended to address issues such as time, technology and economic considerations. The framework will provide a balance between effective, equitable and timely implementation of new or revised air quality standards while providing a mechanism to address implementation issues.

9.0 A Guide for Stakeholders Responding to this Posting

The Ministry welcomes comments on this proposal from all interested parties. Stakeholders are encouraged to provide comments which indicate whether they support or disagree with the above recommendations. It is also important that submissions include the rationale and reasoning supporting the stated positions so that the Ministry can make informed decisions on the proposed standard on the basis of clear, supportable arguments.

If compliance with the proposed standard presents a challenge, please provide information as to the degree of reduction in emission and ground-level concentration that could be, or would have to be, achieved in the operation, facility and/or firm in order to comply. Where it is determined that a proposed standard cannot be achieved immediately, please indicate the earliest possible time frame for compliance with the standard.

During discussions with stakeholders regarding air quality standards, the matter of dispersion models used to estimate air quality concentrations at point of impingement has been raised. In November 1996 and March 2001, the Ministry announced its intent to replace the dispersion models, now shown in the Appendix to Ontario Regulation 346 (1990), with a suite of more refined air dispersion models to calculate POI concentrations. For purposes of replying to this posting, stakeholders may base their responses on concentrations predicted by the models currently included in Reg 346. However, for those who have assessed their POI concentrations using the more advanced US EPA models, this information would be helpful.

The introduction of new models will likely influence all other Ministry air quality standards and guidelines as well as the 15 substances addressed in this posting. To this end, the Ministry acknowledges that, if stakeholders make their comments on these 15 substances based on the Reg. 346 models, any change in the models may result to changes in stakeholders' opinions and comments. The Risk Management Framework for Air (currently under development) may be an appropriate tool used to address implementation issues created by the introduction of new models.

The Ministry also appreciates that responding firms may be committed to, or involved in, developing emission reduction strategies under the federal Strategic Options Processes. Please advise the Ministry, in your submission, whether you are a participant in a Strategic Options Process with the federal government that could result in reductions in the use and/or release of this substance from your operations, facility and/or firm. If so, please identify how these anticipated emission reductions will affect predicted Ground Level Concentrations from your facilities under the existing model.

The foregoing is provided as guidance on the type of information that would assist the Ministry in its ongoing analysis and decision-making in setting an air standard for this substance. In some cases, where it is not feasible to provide all of the information noted within the comment period, the Ministry would appreciate the respondent addressing as many of the issues as possible to ensure an informed decision is made. If stakeholders make no comments about the proposed standards it will be presumed that they have no concerns or will have no difficulty, technically or financially, in complying with the proposed standard.

In addition to the general guidance above, the following Ministry documents provide more detail regarding the type of information that would be considered by the Ministry to assess POI concentrations:

- The documents entitled, "Procedure for Preparing an Emission Summary and Dispersion Modelling Report - June 1998" and the Selected Targets for Air Compliance (STAC) "Technical Guidance to Assist with the Preparation of an Emission

Summary and Dispersion Modelling Report - STAC Technical
Guidance Document – February 2003”;

- MOE Guideline F-14 (formerly 02-01), “Economic Analyses of
Control Documents on Private Sector Enterprises and Municipal
Projects” Economic Services Branch- April 1994.

Comments on these and any other issues relevant to setting air quality standards
for acetonitrile can be sent to:

**Standards Development Branch
Ontario Ministry of Environment
40 St. Clair Avenue West, 7th Floor
Toronto, Ontario
M4V 1M2
Fax: 416 327-2936
E-mail: sdb-ebr@ene.gov.on.ca**

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11.0 Appendix: Agency-Specific Reviews of Air Quality Guidelines

11.1 Agency-Specific Summary: Federal Government of Canada

1. Name of Chemical:

Acetonitrile

2. Agency:

Environment Canada and Health Canada (CEPA)

3. Guideline Value(s):

No guideline has been established. Acetonitrile has not been assessed or evaluated under the first Priority Substance List (PSL1) and is not listed for evaluation under the Second Priority Substance List (PSL2).

4. Application:

The *Canadian Environmental Protection Act* (CEPA) requires the federal Ministers of the Environment and Health to prepare and publish a Priority Substances List (PSL) that identifies substances that may be harmful to the environment or constitute a danger to human health. The Act also requires both Ministers to assess these substances and determine whether they are "toxic" as defined in Section 11 of the Act. The assessment of whether substances are toxic is based on the determination of whether they enter or are likely to enter the Canadian environment in an amount that could lead to exposure of humans or other biota at levels that could cause adverse effects.

Substances that are assessed as "toxic" may be placed on Schedule 1 of the Act and considered for possible development of regulations or guidelines.

5. Documentation Available:

Environment Canada, PSL2 Secretariat, October 1995. Report of the Minister's Expert Advisory Panel on the Second Priority Substances List Under the *Canadian Environmental Protection Act* (CEPA). October, 1995.

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6. Peer Review Process and Public Consultation:

CEPA and Priority Substances List underwent comprehensive public
consultation and review. PSL documents are based on peer-reviewed
literature and are also peer-reviewed prior to being released.

7. Status of Guideline:

Not applicable.

8. Key Risk Assessment Considerations:

Not applicable.

9. Key Risk Management Considerations:

Not applicable.

10. Multimedia Considerations of Guidelines:

Not applicable.

11. Other Relevant Factors:

None.

11.2 Agency-Specific Summary: Federal Government of the United States

1. Name of Chemical:

Acetonitrile. (CAS # 75-05-8)

2. Agency:

US Environmental Protection Agency (Integrated Risk Information System)

3. Guideline Value(s):

No ambient guideline has been established. The US has National Ambient Air Quality Standards (NAAQS) for some "criteria pollutants" (*i.e.* carbon dioxide) but not for toxic air contaminants like acetonitrile. Overall, there are no available listings for ambient guidelines or standards for toxic or hazardous air pollutants on a chemical-by-chemical basis at the federal level. However, under the auspices of the US EPA the Integrated Risk Information System (IRIS) cites inhalation and oral exposure limit information which can be used towards the derivation of ambient air guidelines or standards in other jurisdictions. Currently in IRIS, the inhalation the Reference Concentration (RfC) for acetonitrile is 0.06 mg/m³ or 60 µg/m³. The US EPA has classified acetonitrile as a group D carcinogen (*i.e.*, not classifiable as to human carcinogenicity).

4. Application:

The US EPA has prepared and maintained a database of health risk and regulatory information. This database is called the Integrated Risk Information System (IRIS) and was developed to provide consistent risk information on chemical substances for use in decision-making and regulatory activities. The values reported in IRIS do not represent guidelines or standards.

5. Documentation Available:

US EPA, 1999. Integrated Risk Information System (IRIS) Database. US Environmental Protection Agency, Washington, DC

Key Reference(s):

NTP, 1996. Toxicology and Carcinogenesis Studies of Acetonitrile (CAS # 75-05-8) in F344/N Rats and B6C3F1 Mice (Inhalation Studies). National Toxicology Program. NTP TR 477.

6. Peer Review Process and Public Consultation:

The US EPA makes use of peer-reviewed scientific research data, analyses, and evaluations from various sources, including a variety of public and government agencies from around the world and the published scientific literature. Both the general assessment methodologies and the chemical-specific information found in IRIS undergo extensive scientific and policy reviews, both within the EPA and within other science-based US regulatory agencies. Information is put on IRIS after results of the public review and comments on draft documents/information have been addressed.

7. Status of Guideline:

Current.

8. Key Risk Assessment Considerations:

The US EPA has established an inhalation RfC of 0.06 mg/m³ or 60 µg/m³ for acetonitrile derived from studies conducted in mice by the National Toxicology Program (1996). In this study, six groups of mice were exposed to acetonitrile by inhalation at concentrations of 0, 100, 200, 400, 800 or 1,600 ppm (approximately: 0, 170, 340, 670 1,340, or 2,690 mg/m³) (NTP, 1996). Mortality was observed at concentrations of 670 mg/m³ or greater. All the mice in the 2,690 mg/m³ group died by the fourth week of the study. Toxicity resulting from chronic exposure included increased liver weight and increased incidences of hepatocellular vacuolization and forestomach hyperplasia. As hepatocellular vacuolization was not observed in the mice in the highest concentration group that died, the authors concluded that vacuolization represented the storage of glycogen and was not considered to be an adverse effect. Forestomach hyperplasia is considered to be an adverse effect as it is associated with an increase of inflammatory cells and focal ulcers (at the highest concentrations in female mice). However, the role of inhalation on the development of forestomach hyperplasia is not clear as other exposure routes such as grooming of contaminated fur or mucociliary clearance followed by ingestion are likely to account for a large part of the increased incidence of hyperplasia of the forestomach. Based on this study, the NOAEL is considered to be 60 mg/m³ (adjusted for exposure duration). A similar 13-week study was conducted on rats, but due to limited

histopathological observations in the lower concentration groups, the results were insufficient to identify a NOAEL (NTP, 1996).

The National Toxicology Program also conducted an 111-week study on four groups of mice exposed to acetonitrile by inhalation at concentrations of 0, 50, 100, and 200 ppm (approximately 0, 85, 170, or 340 mg/m³). The exposures were selected based on the 13-week study. Clinical signs and body weight were monitored throughout the study, but hematological parameters were not. No differences in survival, body weight, or liver weight were observed between the treated mice and the control groups. Forestomach hyperplasia was observed to increase significantly at 336 mg/m³ in male mice and at both 168 and 336 mg/m³ for female mice. However, neither a NOAEL nor a LOAEL can be determined from this study, due to the uncertainty of the cause of the forestomach lesions. In a similar two-year study of groups of rats exposed to 0, 100, 200, and 400 ppm (approximately 0, 170, 340, and 680 mg/m³), no adverse effects were found and a NOAEL of 120 mg/m³ (680 mg/m³ adjusted for exposure duration) was identified for the rat (NTP, 1996).

In deriving the RfC for acetonitrile, the US EPA (1999) applied an uncertainty factor (UF) of 100 to the NOAEL of 336 mg/m³ (NOAEL adjusted for exposure duration = 60 mg/m³) to extrapolate between species ($10^{1/2} = 3$), to account for intraspecies extrapolation (10) and to account for database insufficiencies ($10^{1/2} = 3$). A modifying factor (MF) of 10 was used to account for the uncertain role that inhalation may play in causing forestomach lesions which are found in mice that are subchronically and chronically exposed to acetonitrile. These lesions are likely to be the result of grooming contaminated fur although inhalation appears to play a role as well. It appears that grooming of contaminated fur or mucociliary clearance followed by ingestion was likely the primary cause of the increased incidence of forestomach hyperplasia. A study by Wolfe *et al.* (1982) compared the whole-body exposure versus nose-only exposure for rats exposed to radiolabelled fine particles and found that whole-body exposure resulted in the ingestion of 60% of the pelt burden. However, the inhalation of acetonitrile can not be ruled out as a cause of forestomach hyperplasia (US EPA, 1999).

$$\text{RfC} = 60 \text{ mg/m}^3 / (100 * 10) = 0.06 \text{ mg/m}^3 \text{ or } 60 \text{ }\mu\text{g/m}^3$$

Confidence in the principal study, the overall database of toxicological information and the inhalation RfC for acetonitrile is reported as medium. Although the NTP study (1996) utilized appropriate sample sizes, extensive histopathology and detailed data reporting format, haematological parameters were not measured in mice and only at the 15-month interim in rats. The database was given a medium confidence rating because of the uncertain role of inhalation in the development of

forestomach lesions in the mouse study, the lack of evaluation of possible effects of acetonitrile on heart rate, ventilatory parameters and blood pressure as well as the absence of two-generation studies. Since the confidence in both the principal study and the database are rated as medium, the confidence in the RfC is also considered medium.

9. Key Risk Management Considerations:

No information available.

10. Multimedia Considerations of Guidelines:

No adjustment for multimedia exposure is considered in the development for RfCs (for threshold effects) or unit risk values (for non-threshold effects).

11. Other Relevant Factors:

None.

11.3 Agency-Specific Summary: State of California

1. Name of Chemical:

Acetonitrile (CAS # 75-05-8)

2. Agency:

State of California Office of Environmental Health Hazard Assessment (OEHHA); California EPA, Air Resources Board (ARB); California Air Pollution Control Officers Association (CAPCOA)

3. Guideline Value(s):

No health-based concentration limit has been established for acetonitrile.

4. Application:

The Revised 1992 Risk Assessment Guidelines were developed by CAPCOA to provide guidance for the risk assessment procedures which are to be used for the Air Toxics "Hot Spots" Program. This program is based on the California State law *Air Toxics "Hot Spots" Information and Assessment Act* detailed under the Health and Safety Code, Section 44360 *et seq.*, 1987. This Act requires local Air Pollution Control Districts to identify facilities in their area which will conduct risk assessments, outline how such assessments should be prepared and detail how the results are to be used in prioritizing substances for needs assessments will be performed, thereby facilitating comparison and review of such report. The State does not consider these exposure levels to be legally enforceable air quality guidelines or limit values as they should not be employed outside the scope of the program.

The Toxic Air Contaminant Identification List was compiled by the OEHHA and the ARB as part of the State's Air Toxic Program Assembly Bill (AB)-1807. This draft report presents individual summaries detailing the general exposure and health effects for the 244 substances identified on this list. The summaries are not based upon new California EPA evaluations and do not revise California EPA judgements or policies about the potential for these pollutants to cause harm to human health. Although this document identifies risk-based guidance values which have been established or accepted by the OEHHA, the original documentation for such values should be consulted in order to review the conditions under which these values should be reviewed, interpreted and applied.

5. Documentation Available:

CAPCOA, 1993. CAPCOA Air Toxics "Hot Spots" Program. Revised 1992 Risk Assessment Guidelines. Toxics Committee of the California Air Pollution Control Officers Association.

OEHHA, 1997. Technical Support Document for the Determination of Noncancer Chronic Reference Exposure Levels. Office of Environmental Health Hazard Assessment, California Environmental Protection Agency, California, USA.

ARB, 1998. Toxic Air Contaminant Identification List - Summaries (Draft Report). California Environmental Protection Agency - Air Resources Board.

6. Peer Review Process and Public Consultation:

The Draft Toxic Air Contaminant Identification List is currently undergoing an extensive peer-review and is open for public review and comments. The sources which were used to compile the technical summaries for the 244 substances identified on the Toxic Air Contaminants Identification List were taken from existing governmental exposure and health effects databases (eg., HSDB, IRIS etc.) and additional widely recognized reference texts.

The California RfCs, Reference Exposure Levels (RELs) and cancer potency values reported in both the draft Toxic Air Contaminant Identification List and CAPCOA documents were prepared and/or adopted for consideration by the OEHHA after extensive review. The rationales for the derivation of all these values have undergone public review and consultation. Any risk assessment conducted under these guidelines is subject to review by the local district and the OEHHA. In addition, public input plays a key role in the identification and prioritization of the areas and facilities for which risk assessments are required.

7. Status of Guideline:

Not applicable.

8. Key Risk Assessment Considerations:

Acetonitrile is listed on the December 1998 Toxic Air Contaminants List (ARB, 1998) for further assessment.

9. Key Risk Management Considerations:

None.

10. Multimedia Considerations of Guidelines:

The State of California requires risk assessment to consider exposure to certain substances via non-inhalation pathways (specific compounds are listed under Table III-5 in CAPCOA, 1993). Acetonitrile is not one of these substances.

11. Other Relevant Factors:

Acetonitrile is identified by CAPCOA as a quantifiable and reportable substance in any risk assessment undertaken by a facility posting emissions and/or any risk assessment which is required under the "Hot Spots" Program.

11.4 Agency-Specific Summary: State of Massachusetts

1. Name of Chemical:

Acetonitrile (CAS # 75-05-8)

2. Agency:

Commonwealth of Massachusetts, Department of Environmental Protection

3. Guideline Value(s):

Neither a Threshold Effects Exposure Limit (TEL) nor an Allowable Ambient Limit (AAL) exists for acetonitrile.

4. Application:

The TEL and AAL guidelines are to be employed in permitting, compliance and enforcement of the Commonwealth of Massachusetts air quality program. The primary goal of the TELs and AALs developed by MDEP is to protect public health from any air contaminants causing known or potentially deleterious effects. These guidelines were developed without regard to production volume, exposure level, regulatory implication, economic considerations, or control technology issues.

5. Documentation Available:

MDEP, 1990. The Chemical Health Effects Assessment Methodology and the Method to Derive Allowable Ambient Limits. Vol. I and II. Commonwealth of Massachusetts, Department of Environmental Protection, Boston, Massachusetts.

MDEP, 1994. Memorandum from the Office of Research and Standards dated October 20, 1994. This memorandum outlines a number of revisions to the 1990 Chemical Health Effects Assessment Methodology and the Method to Derive Allowable Ambient Air Limits, Commonwealth of Massachusetts, Department of Environmental Protection, Boston, Massachusetts.

MDEP, 1995. Summary Table of Massachusetts Threshold Effects Exposure Limits (TELs) and Allowable Ambient Limits (AALs) for Ambient Air. Commonwealth of Massachusetts, Department of Environmental Protection, Office of Research and Standards, Boston, Massachusetts.

6. Peer Review Process and Public Consultation:

In the development of the Massachusetts ambient air guidelines, peer-reviewed scientific data and analyses from both public and government sources were used. Toxicological information and exposure limits from the following agencies and programs were reviewed: United States Environmental Protection Agency (US EPA), the International Agency for Research on Cancer (IARC), the American National Toxicology Program (NTP), the National Institute of Occupational Safety and Health (NIOSH), the American Conference of Governmental Industrial Hygienists (ACGIH), and the Occupational Safety and Health Administration (OSHA). Internal and external peer-review and public consultation processes have been carried out since 1982.

7. Status of Guideline:

No guideline exists for acetonitrile.

8. Key Risk Assessment Considerations:

The MDEP has developed a policy for establishing air limits. The methodology addresses both threshold and non-threshold effects, with selection of the final AAL based on the most sensitive effect. The process focuses primarily on hazard identification and dose-response assessment.

9. Key Risk Management Considerations:

The selection of the AAL is based on the most sensitive end point of an adverse health effect. The goal of the process is the protection of human health. For carcinogens, the AAL is derived in the MDEP process corresponds to a maximum allowable excess lifetime cancer risk of one in one million (10^{-6}) or less. The process of derivation of air guidelines does not consider technological, economic or enforcement issues.

10. Multimedia Considerations of Guidelines:

A factor of 20% was applied to the adjusted MAOL used as the basis of the TEL guideline to allow for contributions from exposure media other than air. However, the AAL does not consider other sources of exposure.

11. Other Relevant Factors:

None.

11.5 Agency-Specific Summary: State of Michigan

1. Name of Chemical:

Acetonitrile (CAS # 75-05-8)

2. Agency:

State of Michigan Department of Environmental Quality (DEQ)

3. Guideline Value(s):

The Initial Threshold Screening Level (ITSL) is $60 \mu\text{g}/\text{m}^3$ averaged over 24 hours.

4. Application:

Screening levels are used for the implementation of Michigan's Air Toxic Rules (Rules 230-232), which apply to any new or modified process for which an application for a permit to install is required, and which emits a toxic air contaminant (State of Michigan, 1995). There are two basic requirements of the air toxic rules as follows:

- i.) each source must apply the best available control technology for toxics (T-BACT);
- ii.) after the application of T-BACT, the Predicted Ambient Impact (PAI) of each toxic air contaminant cannot exceed its screening level.

The PAI of each toxic air contaminant is determined using the maximum hourly emission rate for that substance from the facility applying for a permit. The PAI is determined by application of a dispersion model or screening method in accordance with specific regulatory provisions (set out in R336.1240 or R336.1241, or both), by a screening method using a Dilution Matrix included in R336.1230 (Table 22), or by a screening method approved by the regulatory authority.

Screening levels for each toxic air contaminant are developed by the Air Quality Division of the DEQ and are applied across the state. They are used in evaluating the acceptability of emissions from new and modified sources of toxic pollutants. The intent is to protect ambient air, but the screening levels are not ambient air standards *per se*. Rather, they are health-based levels which the PAI of emissions from a subject facility cannot exceed. If the PAI exceeds the screening level set for a substance, facility specific physical or operational changes will be required to reduce emissions in order for a permit to be issued.

5. Documentation Available:

State of Michigan, 1989. Final Report of the Michigan Air Toxics Policy Committee: A Proposed Strategy for Processing Air Quality Permit Applications for New Emission Sources of Toxic Air Pollutants. Michigan Department of Natural Resources.

State of Michigan, 1992. R336.1230 Air Toxics from New and Modified Sources.

State of Michigan, 1995. Procedures for Developing Screening Levels. Michigan Department of Natural Resources, Air Quality Division.

State of Michigan, 2001. List of Screening Levels (ITSL, IRSL, and SRSL) for Michigan's Air Toxic Rules. Michigan Department of Environmental Quality, Air Quality Division.

Key Reference(s):

US EPA, 1999. Integrated Risk Information (IRIS) Database. US Environmental Protection Agency, Washington, DC

6. Peer Review Process and Public Consultation:

Peer-reviewed scientific research data and evaluations from various sources were employed in the development of the ITSL. Specifically, information from the US EPA's process for the development of reference concentrations (RfCs), upon which the ITSL for acetonitrile is based, was employed.

7. Status of Guideline:

Current

8. Key Risk Assessment Considerations:

The health assessment methodology used by the DEQ for non-carcinogenic compounds involves determination of an ITSL. The ITSL is a regulatory level used in evaluating the acceptability of emissions from new and modified sources of toxic air pollutants. The ITSL is set at some fraction of the observable threshold dose determined in studies using laboratory animals or from humans. The methodology for determining the ITSL is contained in Rule 232.

The ITSL for acetonitrile was adopted from the RfC developed by the US EPA. The ITSL, which is averaged over 24 hours, equals the inhalation RfC.

9. Key Risk Management Considerations:

None.

10. Multimedia Considerations of Guidelines:

None.

11. Other Relevant Factors:

None.

11.6 Agency-Specific Summary: State of New Jersey

1. Name of Chemical:

Acetonitrile (CAS #75-05-8)

2. Agency:

State of New Jersey, Department of Environmental Protection (NJDEP)

3. Guideline Value(s):

NJDEP has adopted the US EPA's RfC of $60 \mu\text{g}/\text{m}^3$ as their reference concentration for inhalation (RfC) for acetonitrile.

4. Application:

The list of reference concentrations for inhalation is maintained by the Department of Environmental Protection to assist in the development of a risk assessment for permit purposes. Risk screening, as developed by the Air Quality Permitting Program, consists of two levels. The first risk screening level uses information from permit applications and generalised worst case assumptions to estimate non-cancer and cancer risk from inhalation. Sources that fail the first level of screening are submitted to a second risk screening level, which uses additional information and a mathematical dispersion model to more accurately predict risk. In the case of sources that fail both screening levels, the Risk Management Committee makes its recommendation based on a case-by-case evaluation. A refined risk assessment is compulsory for certain categories of sources (coal-fired plant, medical, pathological, industrial or commercial incinerators, *etc.*).

5. Documentation Available:

NJDEP, 1994a. Technical manual 1003-Air Quality Regulation Permitting Program, Bureau of Air Quality Evaluation: Guidance on Preparing a Risk Assessment for Air Contaminant Emissions, New Jersey Department of Environmental Protection, Air Quality Permitting Program, Bureau of Air Quality Evaluation.

NJDEP, 1994b. New Jersey Administrative Code Title 7, Chapter 27, Subchapter 17 - Control and Prohibition of Air Pollution by Toxic Substances.

US EPA, 1999. Integrated Risk Information System (IRIS) Database. US Environmental Protection Agency, Washington, DC.

Key Reference(s):

NTP, 1996. Toxicology and Carcinogenesis Studies of Acetonitrile (CAS # 75-05-8) in F344/N Rats and B6C3F1 Mice (Inhalation Studies). National Toxicology Program. NTP TR 477.

US EPA, 1990. Interim Methods for Development of Inhalation Reference Concentrations (Review Draft). EPA/600/8-90/066A, Office of Research and Development, Washington, DC.

6. Peer Review Process and Public Consultation:

No information.

7. Status of Guideline:

Current.

8. Key Risk Assessment Considerations:

The current RfC derived by the US EPA of 60 $\mu\text{g}/\text{m}^3$ for acetonitrile was adopted by New Jersey.

9. Key Risk Management Considerations:

Risk management issues are referred to the Risk Management Committee of the NJDEP.

10. Multimedia Considerations of Guidelines:

Information submitted by applicants for Refined Risk Assessment is for ambient air only.

11. Other Relevant Factors:

None.

11.7 Agency-Specific Summary: State of New York

1. Name of Chemical:

Acetonitrile (CAS # 75-05-8)

2. Agency:

New York State Department of Environmental Conservation

3. Guideline Value(s):

The Short-term Guideline Concentration (SGC) for acetonitrile is 10 000 $\mu\text{g}/\text{m}^3$ (1-hour average) and the Annual Guideline Concentration (AGC) for acetonitrile is 60 $\mu\text{g}/\text{m}^3$.

4. Application:

The NYSDEC guidelines for the control of toxic ambient air contaminants is intended primarily for use in the decision making process of permitting emissions (6NYCRR Parts 200, 201, 212, and 257), and for the application of certificates of operation for sources of air contamination. The regulatory process used in NYSDEC provides both short- and long-term guidelines to establish appropriate control requirements under existing statutes. The guidelines have been developed to aid the regulatory decision-making process using scientific data and professional judgement. However, they have not been subjected to the same degree of review as applied to an environmental standard.

5. Documentation Available:

NYSDEC, 1991. New York State Air Guideline-1. Guidelines for the Control of Toxic Ambient Air Contaminants. Draft. New York State Department of Environmental Conservation, Division of Air Resources, Albany, New York.

NYSDEC, 2000. DAR-1 (Air Guide-1) AGC/SGC Tables. New York State Department of Environmental Conservation, Division of Air Resources, Albany, New York.

Key Reference(s):

US EPA, 1999. Integrated Risk Information (IRIS) Database. US Environmental Protection Agency, Washington, DC

American Conference of Governmental Industrial Hygienists, 1990-1991. Threshold Limit Values for Chemical Substances and Physical Agents and Biological Exposure Indices. Ohio, Cincinnati.

American Conference of Governmental Industrial Hygienists. 2000. Threshold Limit Values for Chemical Substances and Physical Agents and Biological Exposure Indices. Ohio, Cincinnati.

6. Peer Review Process and Public Consultation:

Peer-reviewed data and computer models were used in the development of the scientific documents supporting the air guidelines. Scientific and professional judgements were employed in the toxicological assessment of contaminant classification and in the screening model analysis.

There are opportunities for public consultation, including the option to review the guidance used in the development of guidelines under certain circumstances and/or the option to develop an ambient air guideline for a contaminant not listed in the current guidelines.

7. Status of Guideline:

Current.

8. Key Risk Assessment Considerations:

Acetonitrile is classified as a moderate toxicity air contaminant (Table III, Appendix C of NYSDEC, 1991). Moderate toxicity air contaminants are defined as those chemicals which are animal oncogens, developmental and reproductive toxicants, genotoxic chemicals and other chemicals posing a health hazard to humans. The criteria used to determine whether a chemical poses a health hazard to humans are:

- i.) those chemicals that when inhaled have caused significant chronic adverse effects in test animals.
- ii.) those chemicals which are irritants to sensitive members of the population at concentrations equal to or below the Threshold Limit Value (TLV-TWA).
- iii.) those chemicals which have:
 - an LD₅₀(dermal) greater than 200 mg/kg but less than 1,000 mg/kg or;
 - an LD₅₀ (inhalation) greater than 200 ppm (336,000 µg/m³) but less than 2,000 ppm (3,360,000 µg/m³) or; an LD₅₀ (oral) greater than 50 mg/kg but less than 500 mg/kg.

The SGC value was derived by dividing the occupational standard ACGIH STEP value by 10 to protect the general population. The AGC was

adopted from the RfC developed by the US EPA. AGC which is averaged over 24 hours equals the inhalation RfC. The Division of Air Resources, NYSDEC, indicated that the SGC may be dropped as the department moves towards the development of air quality regulations (Desantis, 1999).

9. Key Risk Management Considerations:

Specific computer models have been identified by the agency for use in impact screening as required in the permitting process.

10. Multimedia Considerations of Guidelines:

The NYSDEC guideline considers only human airborne to contaminants in air.

11. Other Relevant Factors:

None.

11.8 Agency-Specific Summary: The Netherlands

1. Name of Chemical:

Acetonitrile (CAS # 75-05-8)

2. Agency:

Netherlands Ministry of Housing, Spatial Planning and the Environment

3. Guideline Value(s):

Acetonitrile is not classified under the Netherlands Emission Regulations.

4. Application:

These emission regulations are intended for use by all licensing authorities in the Netherlands in order to standardize the rules by which emissions are regulated in conjunction with licensing. These emission standards are to be applied as the maximum permissible emission concentrations for different waste gas components on a facility specific basis. They are applied to emissions occurring at each source and at the point from which the waste gases leave the processing unit.

Compounds have been categorized into substance classes based on their respective toxicological profiles. There are four substance categories into which compounds are divided (carcinogens, particulates (general), organic or inorganic particulates, and organic or inorganic matter in gaseous or vaporous forms). The emission standard is based on mass flow limit which has been established for each substance class derived from the application of best available technology. When the untreated mass flow rate of a substance or a class of substances exceeds the critical mass flow limit established for that class, the standard in question is applied to the total discharge for all sources emitting the compound or compounds in that class. Untreated mass flow is defined as "the mass of particular single substance or summed masses of substances in the same class emitted per unit of time and before any treatment by means of add-on technology" (Netherlands Emission Regulations Staff Office, 1992).

The environmental quality objectives present effects oriented risk levels which have been established for use in a progressive criteria setting program in the Netherlands. The objective of this program is to reduce the emissions of priority setting substances to a concentration at which the occurrence of adverse effects are considered to be negligible. This program details a long-term environmental quality objective which

establishes a target value below which emissions of priority substances must be maintained. This target value is either set at the naturally occurring background level, or a negligible effects concentration which has been established for that compound based on the available toxicological literature. This progressive approach will require facility-specific emissions to be kept below a limit or guidance value which will eventually be tightened to reach the goal of the target value for the compound in question. These guidance or limit values are either air quality statutory requirements or non statutory regional specific MIC levels.

5. Documentation Available:

NeR Staff Office, 1992. Netherlands Emission Regulations - Air. Netherlands Emission Regulation Staff Office, Bilthoven, The Netherlands.

Netherlands MHSPE, 1994. Environmental Quality Objectives in the Netherlands. A review of environmental quality objectives and their policy framework in the Netherlands. Risk Assessment and Environmental Quality Division, Ministry of Housing, Spatial Planning and the Environment (MHSPE), The Hague, The Netherlands.

6. Peer Review Process and Public Consultation:

The Netherlands Emission Regulations and the Environmental Quality Objectives documents were not peer-reviewed or released for public comment.

7. Status of Guideline:

Not applicable.

8. Key Risk Assessment Considerations:

None.

9. Key Risk Management Considerations:

These Netherlands Emission Regulations standards do not replace existing binding emission or national air quality legal regulations and/or standards. These standards are only to be used as guidance for licensing agencies until the Dutch Emissions Guidelines for the granting of licences is released under the *Environmental Protection Act*.

10. Multimedia Considerations of Guidelines:

None.

11. Other Relevant Factors:

None.

11.9 Agency-Specific Summary: Swedish Institute of Environmental Medicine

1. Name of Chemical:

Acetonitrile (CAS # 75-05-8)

2. Agency:

Swedish Institute of Environmental Medicine

3. Guideline Value(s):

No guidelines.

4. Application:

Air emissions in Sweden are regulated by one of two authorities: i) the regional County Government Boards; or ii) the central authority called the National Licensing Board for Environmental Protection. The guidelines are generally applied to permitting of emissions from industrial, heat and power plants.

5. Documentation Available:

Victorin, K., 1993. Health Effects of Urban Air Pollutants: Guideline Values and Conditions in Sweden. *Chemosphere* 27: 1691-1706.

6. Peer Review Process and Public Consultation:

No information.

7. Status of Guideline:

No information.

8. Key Risk Assessment Considerations:

The Institute of Environmental Medicine has performed a number of health risk evaluations on chemicals found in combustion emissions. In general, the Institute develops air guideline values by taking the lowest-observed-effect-level in humans for that compound and applying a factor ranging from 100 to 1000. For cancer-causing chemicals, air guidelines may be based on a lifetime cancer risk of 1×10^{-5} . No assessments have been carried out for acetonitrile.

9. Key Risk Management Considerations:

No information available.

10. Multimedia Considerations of Guidelines:

No information available.

11. Other Relevant Factors:

None.

11.10 Agency-Specific Summary: World Health Organization (WHO)

1. Name of Chemical:

Acetonitrile (CAS # 75-05-8)

2. Agency:

World Health Organization

3. Guideline Value(s):

None.

4. Application:

None.

5. Documentation Available:

WHO, 1987. Air Quality Guidelines for Europe. WHO Regional Publications, European Series No. 23. World Health Organization, Regional Office for Europe, Copenhagen, Denmark, 426 p.

Key Reference(s):

None.

6. Peer Review Process and Public Consultation:

None.

7. Status of Guideline:

None.

8. Key Risk Assessment Considerations:

None.

9. Key Risk Management Considerations:

None.

10. Multimedia Considerations of Guidelines:

None.

11. Other Relevant Factors:

None.

12.0 Acronyms, Abbreviations and Definitions

AAL	<i>Allowable Ambient Level (Massachusetts)</i>
AAQC	<i>Ambient Air Quality Criteria - used by the Ontario Ministry of Environment to define the potential for causing an adverse effect</i>
ACGIH	<i>American Conference of Governmental Industrial Hygienists - a non-governmental organization which establishes occupational safety exposure limits for workers</i>
AGC	<i>Annual Guideline Concentration (New York State)</i>
AIHA	<i>American Industrial Hygiene Association</i>
CAPCOA	<i>California Air Pollution Control Officers Association</i>
CAS	<i>Chemical Abstracts Service - ascribes a unique, identification (registry) number to each chemical to help clarify multiple listings for the same chemical structure</i>
CEPA	<i>Canadian Environmental Protection Act</i>
CCHOS	<i>Canadian Centre for Occupational Health and Safety</i>
GLC	<i>Ground Level Concentration - the concentration of contaminant predicted by dispersion modelling</i>
HEAST	<i>Health Effects Assessment Summary Tables - prepared by US EPA's Office of Health and Environmental Assessment. HEAST contains risk assessment information on chemicals that have undergone reviews, although generally not as extensive as the reviews conducted under IRIS</i>
HSDB	<i>Hazardous Substances Database</i>
IARC	<i>International Agency for Research on Cancer</i>
IRIS	<i>Integrated Risk Information System - a database published by the US EPA containing risk assessment information on a wide range of chemicals</i>

IRSL	<i>Initial Risk Screening Level</i> - a limit corresponding to a one in a million lifetime risk of cancer used by Michigan for screening new sources of emissions
ITSL	<i>Interim Threshold Screening Level</i> - similar to the IRSL, however, derived from the RfC for non-carcinogens
LOAEL	<i>Lowest-Observed-Adverse-Effect-Level</i>
LC₅₀	The concentration of a substance in the medium (eg., air, water, soil) to which a test species is exposed, that will kill 50% of the population of that given species
LD₅₀	The dose of a substance given to a test species, that will kill 50% of the population of that given species
µg	a microgram, one millionth of a gram
mg	a milligram, one thousandth of a gram
MF	<i>Modifying Factor</i>
MOE/MOEE	The use of MOE or MOEE for the Ministry represents organizational changes which have occurred according to the following timeline: 1973 - 1993/1997 - 2002: <i>Ministry of the Environment</i> , MOE 1993 - 1997/2002: <i>Ministry of Environment and Energy</i> , MOEE
NIOSH	<i>National Institute for Occupational Safety and Health</i> (an agency of the US Department of Health & Human Services)
NOAEL	<i>No-Observed-Adverse-Effect Level</i>
NPRI	<i>National Pollutant Release Inventory</i>
NTP	<i>National Toxicology Program</i> (USA)
OEHHA	<i>Office of Environmental Health Hazard Assessment</i> (California EPA)
OSHA	<i>Occupational Safety and Health Association</i> - a branch of the US Dept of Labour
POI	<i>Point of Impingement</i> - used in conjunction with dispersion modelling to define the area in which the maximum ground level concentration (GLC) of a contaminant is predicted to occur

ppm	parts per million
REL	Either ' <i>Reference Exposure Level</i> ' as used by the California EPA which defines the concentration at or below which no adverse health effects are expected in the general population or ' <i>Recommended Exposure Limit</i> ' used by both NIOSH and ATSDR
RfC	<i>Reference Concentration</i> - an estimate of a daily inhalation exposure not likely to induce deleterious non-cancer health effects during a lifetime
RTECS	<i>Registry of Toxic Effects of Chemical Substances</i> - database maintained by NIOSH
SGC	<i>Short-term Guideline Concentration</i> (New York State)
TLV	<i>Threshold Limit Value</i> - an exposure concentration that should not induce an adverse effect in a work environment
TWA	<i>Time-Weighted-Average</i> - allowable exposure averaged over an 8-hour workday or 40-hour work week
UF	<i>Uncertainty Factor</i>
US EPA	<i>United States Environmental Protection Agency</i>
WHO	<i>World Health Organization</i>
ppm	parts per million
ppb	parts per billion
mg	a milligram, one thousandth of a gram
μg	a microgram, one millionth of a gram
ng	a nanogram, one billionth of a gram

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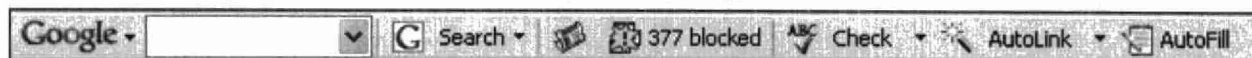
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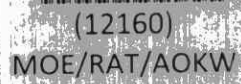


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